

Antiviral drugs that are anti-cancer

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Surprising results show that a class of antiviral drugs blocks the progression of metastatic colorectal cancers that do not respond to any other treatment.

Cancers that reach an advanced stage are extremely difficult to treat, because they are formed of completely degenerated cells, where the most complete anarchy reigns within their chromosomes. Instead of the 23 pairs of chromosomes normally found in a healthy cell, cancer cells can contain 60 or even sometimes 90 chromosomes, some being present in several copies, while others, on the contrary, are completely absent or are formed from fragments originating from different chromosomes.

JUNK DNA

Another frequently observed anomaly in the genetic material of cancer cells is the presence of large amounts of junk DNA, present as repetitive sequences.

Most of this junk DNA, which comes from ancient retroviruses that integrated into the human genome during evolution, is dormant in normal cells but can become very abundant in certain types of cancers (colon, esophagus and lung, among others). The activation of these repetitive sequences in fact generates large quantities of RNA that are subsequently replicated in DNA by an enzyme called reverse transcriptase present in some of these sequences of viral origin.

The repetitive DNA sequences are therefore generated by a reproduction cycle very similar to that of the replication of retroviruses, which causes the accumulation of very large quantities of this DNA within cancer cells. Studies show that the activation of the immune system and the inflammatory response caused by this DNA generated by reverse transcriptase are associated with an increased risk of metastasis.

This therefore raises the interesting possibility that blocking reverse transcriptase using inhibitors commonly used against certain retroviruses (AIDS and hepatitis B viruses) can positively influence tumor progression and the formation of metastases.

BETTER SURVIVAL

To test this possibility, a team of researchers from the Mass General Cancer Center (Boston) and the Memorial Sloan Kettering Cancer Center (New York) administered a reverse transcriptase inhibitor (lamivudine) to 32 patients with resistant metastatic colorectal cancer to all current therapies (1). They observed that despite the very poor prognosis of these patients, lamivudine produced a positive clinical response in 25%, with an average progression-free survival of 150 days (compared to 60 for non-responders). One of the patients even achieved 230 days of survival, which is remarkable considering the seriousness of the condition of these patients.



According to the authors, it is likely that the use of newer and more effective reverse transcriptase inhibitors could further improve this increase in survival.

It therefore seems that in certain cancers, the production of these repetitive DNA sequences does indeed play an important role in the progression of these tumors and that the inhibition of the responsible enzyme, reverse transcriptase, could represent a new avenue of treatment. These results would also explain why patients with AIDS who are treated with therapies containing reverse transcriptase inhibitors have a reduced incidence of certain cancers, in particular those of the breast, prostate and colon (2).

- (1) Rajurkar M et al. Reverse transcriptase inhibition disrupts repeat element life cycle in colorectal cancer. *Cancer Discov.* 2022;12(6): 1462-1481
- (2) Coghill AE et al. Risk of breast, prostate, and colorectal cancer diagnoses among HIV-infected individuals in the United States. *J. Natl Cancer Inst.* 2018;110: 959-966.